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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,524	10/12/2001	Weng Tao	19141-543 Natl.	9720

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EXAMINER	
WILSON, MICHAEL C	

ART UNIT	PAPER NUMBER
1632	9

DATE MAILED: 12/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/830,524	TAO ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *1-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election of Group VII, claim 30, in Paper No. 8 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 8.

Claim 30 is under consideration in this office action.

Priority

This application filed under former 37 CFR 119(e) or 120 lacks the necessary reference to the prior application. A statement reading "This is a Continuation in part of Application No. 09/178869, filed 10-26-98, now US Patent 6,197,294 and PCT/US99/24630, filed 10-21-99." should be entered following the title of the invention or as the first sentence of the specification.

Specification

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

The description of the drawings is not adequate. The heading for each figure should include subfigures. For example, the description of Fig. 1 on pg 5, line 15, should begin –Figure 1A-1C shows...-- instead of "Figure 1 shows...."

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 30 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated cell transfected with a vector comprising a polynucleotide sequence encoding a fusion protein comprising the Fc region of an IgG which is linked at its amino terminal to the transferrin receptor wherein the polynucleotide sequence encoding the fusion protein is operatively linked to a promoter and wherein the fusion protein is expressed on the cell surface, does not reasonably provide enablement for implanting such an isolated cell into a patient for therapy. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claim 30 is directed toward implanting transfected cells in a permselective membrane into a patient, wherein the transformed cells secrete a biologically active molecule. The only use for implanting transfected cells as claimed described in the specification is therapy (pg 20, lines 3-17).

The art of implanting non-transfected cells in a permselective membrane to a patient was known in the art (Uladag, Adv. Drug Delivery, 1993, Vol. 10, pg 115-130). The parameters required to obtain secretion of biologically active protein were dependent upon the cell type, permeability, protein size, molecular weight-cut off of the membrane, number of cells seeded into the membrane and site of implantation (pg 116-117, "Introduction"; pg 126-127, "Biological activity of secreted proteins" and "Future").

The art did not teach obtaining a therapeutic effect by implanting transfected cells into a patient as claimed.

While progress has been made in recent years for gene transfer *in vivo*, vector targeting to desired tissues continues to be unpredictable and inefficient as supported by numerous teachings available in the art. For example, Miller (1995, FASEB J., Vol. 9, pages 190-199) review the types of vectors available for *in vivo* and *ex vivo* gene therapy, and conclude that "for the long-term success as well as the widespread applicability of human gene therapy, there will have to be advances...targeting strategies outlined in this review, which are currently only at the experimental level, will have to be translated into components of safe and highly efficient delivery systems" (page 198, column 1). Deonarain (1998, Expert Opin. Ther. Pat., Vol. 8, pages 53-69) indicate that one of the biggest problems hampering successful gene therapy is the "ability to target a gene to a significant population of cells and express it at adequate levels for a long enough period of time" (page 53, first paragraph). Deonarain reviews new techniques under experimentation in the art that show promise but states that such techniques are even less efficient than viral gene delivery (see page 65, first paragraph

under Conclusion section). Verma (Sept. 1997, Nature, Vol. 389, pages 239-242) reviews vectors known in the art for use in gene therapy and discusses problems associated with each type of vector. The teachings of Verma indicate a resolution to vector targeting has not been achieved in the art (see entire article). Verma also teaches appropriate regulatory elements may improve expression, but it is unpredictable what tissues such regulatory elements target (page 240, sentence bridging columns 2 and 3). Crystal (1995, Science, Vol. 270, page 404-410) also reviews various vectors known in the art and indicates, "among the design hurdles for all vectors are the need to increase the efficiency of gene transfer, to increase target specificity and to enable the transferred gene to be regulated" (page 409).

The specification teaches the transferrin receptor-IgG fusion protein expressing cells (BHK-Fc$_{\Delta}$H) (pg 28, line 18; Figure 5). The specification does not teach any other transformed cells. The specification teaches how to put transformed cells into capsules (pg 21-22) and states that 10^3-10^8 cells are encapsulated, preferably 10^5-10^7 cells are encapsulated (pg 22, lines 3-6) in the method of implantation.

However, the specification does not enable implanting transformed cells into a patient for therapy, particularly cells transfected with DNA encoding the transferrin receptor-IgG fusion protein. The specification does not teach the amount of transferrin receptor-IgG fusion protein secretion (or any other protein) required to obtain a therapeutic effect, how to target the protein to the appropriate cells, the promoter required to obtain therapeutic levels of secretion of the protein or the target cells required to obtain a therapeutic effect. The specification does not overcome the

unpredictability in the art by providing the combination of parameters required to target the protein to the necessary cells, obtain therapeutic levels of the protein or to obtain a therapeutic effect using the claimed method. It would require one of skill undue experimentation to determine the combination of parameters required to obtain a therapeutic effect using any transfected cell implanted in a permselective membrane as claimed. Therefore, the specification does not enable one of skill to use the method claimed for therapy.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 30 is rejected under 35 U.S.C. 102(a) as being anticipated by Cheng (Human Gene Therapy, Sept. 20, 1998, Vol. 9, pg 1995-2003).

Cheng taught implanting cells comprising DNA encoding porcine growth hormone into pigs using microcapsules. The microcapsules are the core and the jacket as claimed and have a permselective membrane as claimed because the microcapsules are "cross-linked" and secrete porcine growth factor (pg 1996, col. 2, 1st and 2nd ¶, pg 1997, col. 1, 2nd ¶, col. 2, 1st full ¶; pg 2000, col. 2).

Claim 30 is rejected under 35 U.S.C. 102(b) as being anticipated by Chang (Human gene therapy, 1993, Vol. 4, pg 433-440).

Chang taught implanting cells comprising DNA encoding human growth hormone into mice using microcapsules. The microcapsules are the core and the jacket as claimed and have a permselective membrane as claimed because the microcapsules are "cross-linked" and secrete human growth factor (pg 434, "Transfection..." and "Encapsulation"; pg 435-434, "Delivery of hGH from encapsulated cell").

Claim 30 is rejected under 35 U.S.C. 102(b) as being anticipated by Ballermann (WO 94/25584, Nov. 10, 1994).

Chang taught implanting cells comprising DNA encoding a biologically active protein into patients using polypropylene fibers to obtain secretion of the biologically active protein into the blood stream (pg 12, 1st ¶, especially lines11-13; pg 16, line 16, through pg 17, line 2). The hollow fibers are the core and the jacket as claimed and have a permselective membrane as claimed because the hollow fibers allow secretion of the protein.

Conclusion

No claim is allowed.

The following Patents are related to the claimed invention:

US Patent 6,506,891 drawn to a nucleic acid sequence encoding a fusion protein comprising the Fc portion of an IgG molecule linked at the amino terminus to a transferrin receptor hinge region.

US Patent 6,225,448 drawn to a fusion protein comprising the Fc portion of an IgG molecule linked at the amino terminus to a transferrin receptor hinge region.

US Patent 6,197,294 drawn to a cell transformed in vitro with a vector comprising DNA encoding a fusion protein comprising the Fc portion of an IgG molecule linked at the amino terminus to a transferrin receptor hinge region.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-0120. The examiner will be moving to the new USPTO location on Jan. 12th, 2004. His new number will be 571-272-0738.

Questions of a general nature relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

If attempts to reach the examiner, patent analyst or Group receptionist are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051.

The official fax number for this Group is (703) 872-9306.

Michael C. Wilson

MICHAEL WILSON
PRIMARY EXAMINER